## REMARKS

Claims 9, 11-13, 15 and 17-19 are all the claims pending in the application. Claim 17 has been amended to correct a minor typographical error. New Claims 18 and 19 have been added, directed to oral administration and dosing of the compound of Formula (I). Support can be found throughout the specification at, for instance, page 38. No new matter has been introduced and entry of the amendment and new claims is respectfully requested.

Claims 9, 11-13, 15 and 17 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over EP 1008588 to Ono Pharmaceutical Co., Inc. ("EP '588"), in view of Sheller et al. ("Sheller"). Applicants traverse for the reasons set forth below.

Independent Claim 9 is directed to a method of treating an allergic disease in a mammal, comprising administering an effective amount of a compound represented by formula (I) or a salt or a solvate thereof.

New independent Claim 18 is directed to a method of treating an allergic disease in a mammal, comprising orally administering a compound represented by formula (I) or a salt or a solvate thereof in an amount of 1 μg to 100 mg per dose one or more times a day, or parenterally administering the compound represented by Formula (I) or a salt or a solvate thereof in an amount of 0.1 ng to 10 mg per dose one or more times a day.

Sheller does not teach that misoprostol can be used to treat atopic asthma, or any other disease, and therefore does not disclose the subject matter claimed in the present application. Sheller does not indicate the amount of dosage of Formula (I) that would be required to treat atopic asthma, as recited in Claim 18. Moreover, Sheller does not give any disclosure as to the means of administration of the compound, that would be appropriate for treating atopic asthma.

First, Sheller does not disclose that misoprostol can be used to treat atopic asthma. In this regard, Sheller discloses that misoprostol was given to atopic asthmatic volunteers to see if misoprostol, when given chronically, could influence the release of mediators associated with the late response to allergic challenge (see page 186, third full paragraph). The authors of Sheller found that misoprostol suppresses the allergen-induced release of IL-5 into the airway. However,

there is nothing in Sheller that teaches that a reduction of IL-5 results in a reduction of the allergic response.

Further, one of ordinary skill in the art would understand that a reduction of IL-5 does not necessarily correlate with a reduction of the symptoms of atopic asthma. Rather, a reduction in IL-5 may be too late in the allergic reaction cascade to stop the cells that have already been activated. Sheller fails to address this point. Moreover, Sheller states that the failure of misoprostol to suppress eosinophils could be interpreted in several ways, and, "the effect of misoprostol on acute and late bronchoconstriction is not known." See page 191, second paragraph.

Sheller describes that misoprostol suppresses production of IL-5 (see p. 186, third full paragraph), without affecting the amount of cysLT, eosinophilic cationic protein and eosinophil (see p. 190, first full paragraph). IL-5 relating to late phase reaction of allergy is produced in and released from T-cells (Th2) after antigen stimulation and induces inflammation by accumulating eosinophiles at inflammation sites. That is, if accumulation of eosinophiles can be suppressed by inhibiting production or release of IL-5, allergic reaction will be suppressed.

Misoprostol, whose effect of suppressing production of IL-5 is acknowledged, is unlikely to suppress accumulation of eosinophiles. Therefore, it is unlikely that misoprostol can be said to have an effect of suppressing allergic reaction. It is important for the treatment of allergic diseases to prevent the transfer of eosinophiles to inflammation sites and to prevent the accumulation of eosinophiles in inflammation sites. Without an effect of suppressing accumulation of eosinophiles, misoprotol cannot be declared as having an effect of suppressing an allergic reaction. Thus, one of ordinary skill in the art would likely conclude that Sheller does not show an antiallergic effect of misoprotol.

At page 3 of the Office Action, the Examiner asserts that "Sheller et al. teach that misoprostol is effective in treating atopic asthma...via signaling through EP3 receptor". However, *see* Sheller at page 190, first paragraph, where it is described that "These effects reflect signaling through EP2, EP4, or EP3 receptors." Sheller does not clearly show that the

effect of misoprostol is expressed through the EP3 receptor. In this regard, although misoprotol has affinity with EP2, EP3 and EP4 receptors, there is no teaching in Sheller as to which receptor the effect of suppressing production of IL-5 is expressed through. Thus, in order to clarify and confirm through which receptor the effect is expressed, additional experiments utilizing compounds specific to the receptors are required.

Further, the present invention shows that an agonist drug specific to an EP3 receptor reduces the number of eosinophiles and neutrophils and that the EP3 receptor participates in allergic reactions. If it can be confirmed that the agonist drug specific to EP3 receptor suppresses accumulation of eosinophiles while misoprotol does not, it may be inferred that the effect of misoprotol is not expressed through the EP3 receptor.

Therefore, the antiallergic action of the agonist drug specific to EP3 receptor according to the present invention, which has an effect of suppressing the accumulation of eosinophile, unlike misoprotol, could not have been easily expected by the Sheller reference.

In light of the above, neither EP '588 alone, or in view of Sheller, teach or suggest that EP3 agonist can be used to treat an allergic disease, as claimed in the present invention. Thus, it is respectfully requested that the rejection over 35 U.S.C. § 103 be withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

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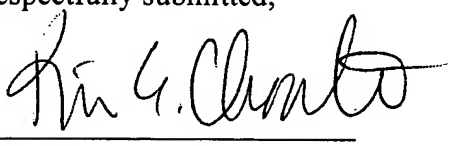
Respectfully submitted,



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